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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
AFREMOVA, VERA	

ART UNIT	PAPER NUMBER
1657	

NOTIFICATION DATE	DELIVERY MODE
06/10/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PTO-PAT-Email@rfem.com

Office Action Summary	Application No.	Applicant(s)	
	10/562,734	NORDLUND ET AL.	
	Examiner	Art Unit	
	Vera Afremova	1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 February 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) *16 and 17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-15 as amended (2/23/2009) are under examination in the instant office action.

Claims 16 and 17 were withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected claims, there being no allowable generic or linking claim. Election was made without traverse (8/06/2008).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2 and 4-15 as amended remain rejected under 35 U.S.C. 102(b) as being anticipated by US 5,506,121 (Skerra et al).

Claims are directed to a method of identifying a cell colony which expresses a soluble target protein wherein the method comprises steps of (a) subjecting said cell colony to conditions which are capable of causing lysis thereof; (b) filtering the lysate of step (a) through a filter having pores which allow only soluble proteins to pass through the filter; and (c) detecting target protein which has passed through the filter, wherein the target is not detected on the basis of its own enzymatic activity. Some claims are further drawn to the lysis being a native lysis that is carried out by using a lysis buffer. Some claims are further drawn to the target protein that is fused to a protein or polypeptide tag including His tag. Some claims are further drawn to identifying or detecting soluble proteins in the filtrate using antibodies and/or fusion tags including tag acting as substrate for enzymatic detection. Some claims are further drawn to the

use of filter with pore size between 0.1 and 1.5 μm. Some claims are further drawn to transfer of colonies from growth media to filter before lysis. Some claims are further drawn to the filtration step (b) that includes application of a generic force to the filter carrying the colonies.

US 5,506,121 (Skerra et al) discloses a "filter sandwich test" in a method for identifying a cell colony which expresses a soluble target protein (see entire document including example 1 at col. 6-7). The disclosed test method comprises steps of growing cell colonies on a first filter or on a first nitrocellulose filter membrane and transferring the first filter on top of the second filter that is coated with a solution of lysozyme and antigen to antibody of interest, thereby, the reference encompasses steps of (a) subjecting cell colonies (including single separated colonies) to conditions which are capable of causing lysis of cell colonies present on the first upper filter ; (b) filtering the lysate of step (a) through the first filter having pores which allow soluble proteins to pass or to diffuse through the filter; and (c) detecting target protein which has passed through the filter, wherein the target protein is detected with antibody but not on the basis of its own enzymatic activity. The disclosed filtration step includes application of a generic gravitational force from top filter to the bottom capture filter in the "filter sandwich test". The cited method encompasses detection of target protein(s) that are fused to a protein or polypeptide tag including His (see abstract, for example). The cited method encompasses identifying or detecting soluble proteins in the filtrate using antibodies (see col.7, line 3) and/or fusion tags including tag acting as substrate for enzymatic detection (see col.7, line 23). The cited method encompasses the use of nitrocellulose filter membrane that is a filter having pore size within the claimed ranges in view of applicant's disclosure, for example: see instant specification page 10, line 9 or fig. 2. The cited method encompasses transfer of colonies from a growth media to a

lysis filter before subjecting to lysis and further capturing the filtrate on solid support of the second "capture" filter .

Thus, the cited method comprises identical active steps and identical structural elements as required by the claimed method. Therefore, the cited patent anticipates the claimed invention.

Claims 1-15 as amended remain rejected under 35 U.S.C. 102(b) as being anticipated by Knaust et al. (IDS reference; Analytical Biochemistry. 2001, 297:79-85) as explained in the prior office action and repeated herein.

Claims are directed to a method of identifying a cell colony which expresses a soluble target protein wherein the method comprises steps of (a) subjecting said cell colony to conditions which are capable of causing lysis thereof; (b) filtering the lysate of step (a) through a filter having pores which allow only soluble proteins to pass through the filter; and (c) detecting target protein which has passed through the filter, wherein the target is not detected on the basis of its own enzymatic activity. Some claims are further drawn to the lysis being a native lysis that is carried out by using a lysis buffer or by freeze thawing colonies. Some claims are further drawn to the target protein that is fused to a protein or polypeptide tag including His tag. Some claims are further drawn to identifying or detecting soluble proteins in the filtrate using antibodies and/or fusion tags including tag acting as substrate for enzymatic detection. Some claims are further drawn to the use of filter with pore size between 0.1 and 1.5 μm. Some claims are further drawn to transfer of colonies from growth media to filter before lysis. Some claims are further drawn to the filtration step (b) that includes application of a generic force to the filter carrying the colonies.

The reference by Knaust et al. teaches a method of identifying a cell colony which expresses a soluble target protein wherein the method comprises steps of (a) subjecting cell originating from a single cell colony to conditions which are capable of causing lysis; (b) filtering the lysate of step (a) through a filter having pores which allow only soluble proteins to pass through the filter; and (c) detecting target protein which has passed through the with anti-RGS-His antibody (see entire document including abstract and figure 2). The lysis is carried out by using a lysis buffer and/or by freeze thawing (figure 2). The filter appears to have same pore size at least for the reason of filtration and detection same soluble proteins as intended for the claimed method. The cell colonies or cell mass is transferred from growth media to lysis filter before lysis as encompassed by the instant claims. The filtration step includes application of a force including gravitation and vacuum manifold (figure 2). Thus, the cited method comprises identical active steps and identical structural elements as required by the claimed method. Therefore, the cited reference anticipates the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-15 as amended remain rejected under 35 U.S.C. 103(a) as being unpatentable over US 5,506,121 (Skerra et al) and Knaust et al. (IDS reference; Analytical Biochemistry. 2001, 297:79-85) as explained in the prior office action and repeated herein.

Claims as above.

The cited documents US 5,506,121 (Skerra et al) and Knaust et al. are relied upon as explained above for the teaching of the methods of identifying cell colonies expressing soluble target proteins wherein the method comprises steps of (a) subjecting cell colony(ies) to conditions which are capable of causing lysis thereof; (b) filtering the lysate of step (a) through a filter having pores which allow only soluble proteins to pass through the filter; and (c) detecting target protein which has passed through the filter, wherein the target is not detected on the basis of its own enzymatic activity. The soluble target proteins are detected with antibodies as disclosed by the cited references. The cited references disclose detection of soluble proteins having same generic tags as encompassed by the claims including His tag. The cell lysis in the method of US 5,506,121 (Skerra et al) is caused by lysozyme or buffer. The cell lysis in the method of Knaust et al. is caused by both lysing buffer and/or freeze thawing.

Thus, the cited documents taken as a whole teach and/or suggest all claimed limitations.

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to apply either lysing buffer or freeze thawing cells in order to lyse cell and to liberate soluble proteins with a reasonable expectation of success in filtrating and detecting soluble proteins in the method of identifying cell colonies expressing soluble target proteins as taught and/or suggested by the cited references. Thus, the claimed invention as a whole was clearly *prima facie* obvious, especially in the absence of evidence to the contrary.

The claimed subject matter fails to patentably distinguish over the state art as represented be the cited references. Therefore, the claims are properly rejected under 35 USC § 103.

Response to Arguments

Applicant's arguments filed 2/23/2009 have been fully considered but they are not persuasive.

With regard to the claim rejection under 35 U.S.C. 102(b) as being anticipated by US 5,506,121 (Skerra et al) applicants argue that the method of the cited reference does not comprises a step of lysis (response pages 9-11). This argument is not found persuasive for the very least reason that the claimed method encompasses a "native" lysis (claim 2) which allows capturing a soluble protein expressed by a growing colony of cells. Although lysozyme might be used by applicants as a lysing agent (page 7), the claims do not require so. In the cited method, a protein separated from the cells as result of a "native" lysis is diffused or filtered through the upper grow membrane to the lower capture membrane and further detected. Thus, the cited method comprises same steps as presently claimed.

Applicant also appear to argue that there might not be any lysis (including "native" lysis) in the cited method because the upper membrane with the growing cells is kept for further evaluation (cell proliferation) after capturing the proteins diffused into lower capture membrane (page 12). However, the claimed method does not require that all cells in the cell colony are lysed and rendered dead and that the lysate of the whole cell colony is collected and/or filtered.

Applicant also argue (page 13) that the claimed method requires the use of "a force" (claim 13) to pull protein through the filter. Yet, the claimed force and some additional force as argued are generic. Thus, a gravitational force that allows protein to pass from upper membrane to the lower capture membrane in the method of the cited reference is not different from a generic force in the claimed step of filtering.

With regard to the claim rejected under 35 U.S.C. 102(b) as being anticipated by Knaust et al. applicants argue that the method of the cited reference encompasses the lysis of cells in the liquid medium and, thus, cell colony lysis is not contemplated. This argument is not found persuasive for the very least reason that the claimed method does not exclude the lysis of cells in a liquid medium. Further, the cited reference clearly contemplates analysis of a single colony or "1 single colony/well", for example: see page 82, col.1, line 2.

With regard to the claim rejection under 35 USC § 103 applicants argue that neither of the two cited references discloses or suggests that lysis of cells and filtration of lysates can be carried out directly on colonies of cells and this direct lysis step, which is not taught or suggested in either document, has enabled the development of the present method, which can operate on large numbers of variants, is inexpensive and has a high reliability in predicting soluble variants of proteins. Yet, cited references encompass and/or disclose cell lysis as claimed (native or by using freeze/thawing) within the broadest meaning of the instant claims as explain for each reference above. The cited references also encompass and disclose analysis of lysates (or partial lysates) obtained/derived from a single colony of cells as explain for each reference above. The claimed subject matter fails to patentably distinguish over the state art as represented be the cited references. Therefore, the claims are properly rejected under 35 USC § 103.

No claims are allowed.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vera Afremova whose telephone number is (571) 272-0914. The examiner can normally be reached from Monday to Friday from 9.30 am to 6.00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon P. Weber, can be reached at (571) 272-0925. The fax phone number for the TC 1600 where this application or proceeding is assigned is (571) 273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Technology center 1600, telephone number is (571) 272-1600.

/Vera Afremova/

Primary Examiner, Art Unit 1657